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Drug Enforcement Administration

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- JULY 2010 -

- SCHEDULING UPDATE –

[Editor's Preface: The following notice has been edited for *Microgram Bulletin*. See the Federal Register: June 29, 2010 (Volume 75, Number 124) (Rules and Regulations) (Page 37295-37299) for the complete text of the ruling.]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-305F] RIN 1117-AB16

Control of Immediate Precursor Used in the Illicit Manufacture of Fentanyl as a Schedule II Controlled Substance

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Final Rule.

SUMMARY: The Drug Enforcement Administration (DEA) is designating the precursor chemical, 4-anilino-N-phenethyl-4-piperidine (ANPP) as an immediate precursor for the schedule II controlled substance fentanyl under the definition set forth in 21 U.S.C. 802(23). Furthermore, DEA is finalizing the control of ANPP as a schedule II

substance under the Controlled Substances Act (CSA), pursuant to the authority in 21 U.S.C. 811(e), which states that an immediate precursor may be placed in the same schedule as the controlled substance it produces, without regard to the procedures required by 21 U.S.C. 811(a) and (b) and without regard to the findings required by 21 U.S.C. 811(a) and 812(b).

ANPP is the immediate chemical intermediary in the synthesis process currently used by clandestine laboratory operators for the illicit manufacture of the schedule II controlled substance fentanyl. In 2005 and 2006, the distribution of illicitly manufactured fentanyl caused an unprecedented outbreak of hundreds of fentanyl-related overdoses in the United States. DEA believes that the control of ANPP as a schedule II controlled substance is necessary to prevent its diversion as an immediate chemical intermediary for the illicit production of fentanyl.

DATES: This rulemaking becomes effective August 30, 2010.

FOR FURTHER INFORMATION CONTACT: Christine A. Sannerud, Ph.D., Chief, Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, 8701 Morrissette Drive, Springfield, VA 22152 at (202) 307-7183.

SUPPLEMENTARY INFORMATION:

The DEA is extremely concerned with the recent increase in the illicit manufacture and distribution of fentanyl, which has resulted in hundreds of fentanyl-related overdoses and fentanyl-related deaths in several areas of the country. Therefore, on April 9, 2008, DEA published a Notice of Proposed Rulemaking (NPRM) [73 FR 19175] to designate the precursor chemical, 4-anilino-N- phenethyl-4-piperidine (ANPP) as an immediate precursor for the schedule II controlled substance fentanyl under the definition set forth in 21 U.S.C. 802(23). This rulemaking finalizes that NPRM.

Under the immediate precursor provision in 21 U.S.C. 811(e), DEA may schedule an immediate precursor "without regard to the findings required by" section 811(a) or section 812(b) and "without regard to the procedures" prescribed by section 811(a) and (b). Because of the authority in section 811(e), DEA need not address the "factors determinative of control" in section 811 or the findings required for placement in schedule II in section 812(b)(2).

This rulemaking finalizes two actions. It (1) designates the precursor chemical ANPP as an immediate precursor for the schedule II controlled substance fentanyl under the definition set forth in 21 U.S.C. 802(23); and (2) controls ANPP as a schedule II substance pursuant to the authority in 21 U.S.C. 811(e).

Background

Fentanyl is a schedule II controlled substance. Fentanyl and analogues of fentanyl are the most potent opioids available for human and veterinary use. Fentanyl produces opioid effects that are indistinguishable from morphine or heroin, but fentanyl has a greater potency and a shorter duration of action. Fentanyl is approximately 50 to 100 times more potent than morphine and 30 to 50 times more potent than heroin, depending on the physiological or behavioral measure, the route of administration, and other factors.

The legitimate medical use of fentanyl is for anesthesia and analgesia, but fentanyl's euphoric effects are highly sought after by narcotic addicts. Fentanyl can serve as a direct pharmacological substitute for heroin in opioid-dependent individuals. Fentanyl is a very dangerous substitute for heroin, however, because the amount that produces a euphoric effect also induces respiratory depression. Furthermore, due to fentanyl's greater potency, illicit drug dealers have trouble adjusting ("cutting") pure fentanyl into non-lethal dosage concentrations. Heroin users similarly have difficulty determining how much to take to get their "high" and sometimes mistakenly take a lethal quantity of the fentanyl. Unfortunately, only a slight excess of fentanyl can be, and is often, lethal because the resulting level of respiratory depression is sufficient to cause the user to stop breathing.

Illicit Fentanyl-Related Deaths

In 2005 and 2006, DEA saw a sharp increase in the seizures of illicit fentanyl. The distribution of illicit fentanyl or illicit fentanyl combined with heroin or with cocaine (i.e., a "speedball") resulted in an outbreak of hundreds of confirmed and suspected fentanyl-related overdose deaths in the United States since April 2005, according to the

Centers for Disease Control and Prevention and medical examiners representing numerous cities and counties across the United States. DEA terms fentanyl-related deaths "suspected" until confirmed through the completion of an autopsy, a positive toxicological testing result for fentanyl in the blood and the reporting of the death to the DEA.

To address this emergency health situation, DEA published an Interim Final Rule, "Control of a Chemical Precursor Used in the Illicit Manufacture of Fentanyl as a List I Chemical" (72 FR 20039, April 23, 2007), followed by a Final Rule (73 FR 43355, July 25, 2008), to control N-phenethyl-4-piperidone (NPP), the chemical precursor to ANPP, as a List I chemical. As DEA discussed extensively in that Interim Final Rule, at least 972 confirmed fentanyl-related deaths, and 162 suspected fentanyl-related deaths, mostly in Delaware, Illinois, Maryland, Michigan, Missouri, New Jersey, and Pennsylvania were initially reported to the DEA. The number of fentanyl- related deaths significantly decreased after October 2006 and continued at lower levels following control of the precursor NPP in 2007.

From the information and data collected, there is a strong indication that the fentanyl in these confirmed and suspected fentanyl- related deaths is the result of illicitly manufactured fentanyl, rather than from fentanyl diverted from legal pharmaceutical manufacturers. Forensic testing of seized fentanyl drug exhibits can identify manufacture procedure markers such as benzylfentanyl and ANPP. The forensic data suggests that most of these fentanyl-related deaths are from fentanyl illicitly manufactured by the procedure called the Siegfried method, discussed in DEA's Interim Final Rule, which uses NPP/ANPP.

Synthesis of Fentanyl

DEA has determined from the forensic testing of seized illicit fentanyl that two primary synthesis routes (i.e., the Janssen synthesis route and the Siegfried method) are being used to produce fentanyl clandestinely. In 1965, Janssen Pharmaceutical patented the original synthesis procedure for fentanyl. The Janssen synthesis route is difficult to perform and is beyond the rudimentary skills of most clandestine laboratory operators. Only individuals who have acquired advanced chemistry knowledge and skills have successfully used this synthesis route. Forensic laboratories can determine whether fentanyl was manufactured illicitly by the Janssen route by detecting the impurity benzylfentanyl in the tested fentanyl drug exhibit.

In the early 1980s, an alternate route for fentanyl synthesis was published in the scientific literature; it uses N-phenethyl-4- piperidone (NPP) as the starting material. The NPP synthesis route is described on the Internet and is referred to as the Siegfried method. The chemical intermediary ANPP is produced during the synthesis and is the immediate precursor used in the illicit manufacture of fentanyl in the last stage of the Siegfried method. The Chemical Abstracts Service Registry Number \1\ (CASRN) for ANPP is 21409-26-7. The detection of the impurity 4-anilino-N-phenethyl-4-piperidine (ANPP) without the presence of benzylfentanyl in the fentanyl drug exhibit suggests that the fentanyl was manufactured by the Siegfried method (or a modified version) that produces the precursor ANPP and then converts ANPP directly to fentanyl. (A small amount of ANPP is not consumed in the last reaction in the synthesis, and thus a trace amount of ANPP remains in the fentanyl.)

[\1\ The Chemical Abstracts Service Registry Number (CASRN) is created by the Chemical Abstracts Service (CAS) Division of the American Chemical Society and is part of an automated information system housing data and information on specific, definable chemical substances. The CASRN provides consistent and unambiguous identification of chemicals and facilitates sharing of chemical information.]

The increase in street-level fentanyl may be the result of the relative ease with which fentanyl can be produced via the Siegfried method and the widespread distribution of the Siegfried method on the Internet. Preliminary data indicate that the majority of the deaths in the 2005-2006 fentanyl outbreak have resulted from the distribution of illicit fentanyl made by the Siegfried method and marked by traces of ANPP rather than benzylfentanyl.

Role of ANPP in Synthesis of Fentanyl

Since 2000, four of the five domestic fentanyl clandestine laboratories seized by law enforcement agents have used the Siegfried method or a modified version of the Siegfried method in manufacturing fentanyl. The amount of illicit fentanyl and precursor chemicals found at these four laboratories could have generated a total of 5,800 grams of illicit fentanyl. Since fentanyl is potent in sub-milligram quantities, the subsequent "cutting" of 5,800 grams of illicit fentanyl would be sufficient to make about 46 million fentanyl doses.

The precursor chemical NPP is the starting material utilized in the Siegfried method of synthesizing fentanyl, both in industry and in illicit drug laboratories. Under a separate rulemaking first published as an interim rule on April 23, 2007 (72 FR 20039), followed by a final rule on July 25, 2008 (73 FR 43355), DEA has controlled the precursor NPP as a List I chemical under the regulatory control provisions of the CSA (21 CFR part 1300).

During the production process, the starting material, NPP, is subjected to a series of chemical reactions in order to produce the intermediary chemical ANPP. The ANPP is then subjected to a simple chemical reaction resulting in the synthesis of fentanyl. DEA has not identified any industrial uses for ANPP and believes that ANPP is only produced as a chemical intermediary in the production of fentanyl, either in the legitimate production of pharmaceutical fentanyl or the illicit production of fentanyl in clandestine laboratories. ANPP is, therefore, an immediate chemical intermediary in the synthesis of fentanyl and is produced primarily for this purpose.

DEA is controlling ANPP as a schedule II controlled substance in an effort to prevent its use in production of illicit fentanyl. DEA believes control is necessary to prevent unscrupulous chemists from synthesizing and distributing ANPP (as an unregulated material), and selling it through the Internet and other channels to individuals who may wish to acquire an unregulated precursor for fentanyl synthesis. DEA believes this action is also advisable in order to deter the theft of ANPP from legitimate pharmaceutical firms where it is generated in the course of fentanyl production. It has been determined by DEA's Office of Forensic Sciences that ANPP can also be produced through synthetic pathways that do not require NPP as the starting material. Therefore, DEA believes that controlling ANPP directly is necessary to prevent the illicit production of fentanyl.

Designation as an Immediate Precursor

Under 21 U.S.C. 811(e), the Attorney General may place an immediate precursor into the same schedule as the controlled substance that the immediate precursor is used to make. The substance must meet the requirements of an immediate precursor under 21 U.S.C. 802(23). The term "immediate precursor" as defined in 21 U.S.C. 802 (23) means a substance:

(A) Which the Attorney General has found to be and by regulation designated as being the principal compound used, or produced primarily for use, in the manufacture of a controlled substance;

(B) which is an immediate chemical intermediary used or likely to be used in the manufacture of such controlled substance; and

(C) the control of which is necessary to prevent, curtail, or limit the manufacture of such controlled substance.

DEA finds that ANPP meets the three criteria for the definition of an immediate precursor under 21 U.S.C 802 (23). First, DEA finds that ANPP is produced primarily for use in the manufacture of the schedule II controlled substance fentanyl. As stated in the preceding section, under the Siegfried method, ANPP is typically produced from the starting material NPP and is then subjected to a simple one-step chemical reaction to obtain the schedule II controlled substance fentanyl. DEA has not identified any industrial or other uses for ANPP and believes that it is produced primarily during the synthesis of fentanyl.

Second, DEA finds that ANPP is an immediate chemical intermediary used in the manufacture of the controlled substance fentanyl. As stated earlier, ANPP is produced as an intermediary in the fentanyl synthetic pathway. After it is synthesized, the ANPP is subjected to a simple chemical reaction that converts it directly to fentanyl.

Third, DEA finds that controlling ANPP is necessary to prevent, curtail, and limit the unlawful manufacture of the controlled substance fentanyl. As noted above, DEA believes this action is necessary to assist in preventing the possible theft of ANPP from legitimate pharmaceutical firms where it is a chemical intermediary generated for fentanyl production. As a schedule II substance, ANPP will be safeguarded to the same degree that pharmaceutical firms now safeguard the fentanyl that they produce. DEA believes this increased level of security is necessary to prevent diversion of ANPP.

As noted previously, ANPP can also be produced through synthetic pathways that do not require NPP as the precursor material. Accordingly, DEA believes control is necessary to prevent unscrupulous chemists from synthesizing ANPP and selling it (as an unregulated material) through the Internet and other channels to individuals who may wish to acquire an unregulated precursor for fentanyl synthesis, in order to circumvent the

regulation of NPP as a List I chemical.

DEA believes that the control of ANPP is necessary to prevent its production and use in the illicit production of fentanyl. Therefore, DEA is designating ANPP as an immediate precursor of fentanyl pursuant to 21 U.S.C. 802 (23) and 21 U.S.C. 811(e).

Placement in Schedule II--Findings Required Under CSA Immediate Precursor Provisions

Under the authority in 21 U.S.C. 811(e), once ANPP is designated as an immediate precursor under 21 U.S.C. 802(23), it may be placed directly into schedule II (or a schedule with a higher numerical designation). The immediate precursor provision in 21 U.S.C. 811(e) permits DEA to schedule an immediate precursor "without regard to the findings required by" section 811(a) or section 812(b) and "without regard to the procedures" prescribed by section 811(a) and (b). Accordingly, DEA need not address the "factors determinative of control" in section 811(c) \2\ or the findings required for placement in schedule II in section 812(b)(2).\3\

[\2\ Under administrative scheduling of a substance pursuant to 21 U.S.C. 811(c), DEA must consider the "factors determinative of control." The DEA must consider the following factors with respect to each drug or other substance proposed to be controlled in a schedule:
(1) Its actual or relative potential for abuse;
(2) Scientific evidence of its pharmacological effect, if known; (3) The state of current scientific knowledge regarding the drug or other substance;
(4) Its history and current pattern of abuse;
(5) The scope, duration, and significance of abuse;
(6) What, if any, risk there is to the public health;
(7) Its psychic or physiological dependence liability; and
(8) Whether the substance is an immediate precursor of a substance already controlled.
21 U.S.C. 811(e) specifies that none of these factors must be considered, however, in the control of an "immediate precursor."]

[\3\ The findings for schedule II include (A) the drug or other substance has a high potential for abuse; (B) the drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions; and (C) abuse of the drug or other substance may lead to severe psychological or physical dependence.]

Based on the finding that ANPP is an "immediate precursor" for fentanyl, DEA is hereby placing ANPP directly into schedule II.

NPRM Comments

[Editor's Note: See the Federal Register for comments received and DEA's response to said comments.]

Requirements for Handling Schedule II Substances

[Editor's Note: See the Federal Register for requirements for handling schedule II substances.]

Regulatory Certifications

[Editor's Note: See the Federal Register for all regulatory certifications.]

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is amended as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: **21 U.S.C. 811**, **812**, **871**(b) unless otherwise noted.

2. Section 1308.12 is amended by adding a new paragraph (g)(3) to read as follows:

Sec. 1308.12 Schedule II.

* * * * *

(g) * * *

(3) Immediate precursor to fentanyl:

(i) 4-anilino-N-phenethyl-4-piperidine (ANPP)..... 8333

(ii) [Reserved]

Dated: June 19, 2010.

Michele M. Leonhart,
Deputy Administrator.

[FR Doc. 2010-15520 Filed 6-28-10; 8:45 am]

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- SCHEDULING UPDATE –

[Editor's Preface: The following notice has been edited for *Microgram Bulletin*. See the Federal Register: June 29, 2010 (Volume 75, Number 124) (Rules and Regulations) (Page 37300-37301) for the complete text of the ruling.]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-313F] RIN 1117-AB26

Correction of Code of Federal Regulations: Removal of Temporary Listing of Benzylfentanyl and Thenylfentanyl as Controlled Substances

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Final Rule.

SUMMARY: This rulemaking corrects Title 21 Code of Federal Regulations (CFR) by deleting regulations which list the substances benzylfentanyl and thenylfentanyl as being temporarily subject to schedule I controls under the emergency scheduling provisions of the Controlled Substances Act (CSA). The temporary scheduling of benzylfentanyl and thenylfentanyl expired on November 29, 1986. DEA determined that these compounds were both essentially inactive, with no evidence of abuse potential. As such, these compounds are no longer schedule I controlled substances and all references to these compounds are being deleted from DEA regulations.

DATES: This rulemaking becomes effective June 29, 2010.

FOR FURTHER INFORMATION CONTACT: Christine A. Sannerud, PhD, Chief, Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, 8701 Morrissette Drive, Springfield, VA 22152 at (202) 307-7183.

SUPPLEMENTARY INFORMATION: The CSA was amended by the Comprehensive Crime Control Act of 1984 (Pub. L.98-473) which became effective on October 12, 1984. This Act included a provision (21 U.S.C. 811(h)) which allows the DEA Administrator to place a substance, on a temporary basis, into schedule I when necessary to avoid an imminent hazard to the public safety. This emergency scheduling authority permits scheduling a substance that is not currently controlled, is being abused, and is a risk to the public health while the formal rulemaking procedures (21 U.S.C. 811) described in the CSA are being conducted. A temporary scheduling order may be issued for one year with a possible extension of up to six months if formal scheduling procedures have been initiated. The proposal and order are published in the Federal Register as are the proposals and orders for formal scheduling. The emergency scheduling authority was given to DEA in an effort to streamline the scheduling process in response to the growing problem of controlled substance analogues (``designer drugs'').

On October 29, 1985, DEA published a Final Rule (50 FR 43698) which temporarily placed Acetyl-alpha-methylfentanyl, Alpha- methylthiofentanyl, Beta-hydroxyfentanyl, Beta-hydroxy-3- methylfentanyl, 3-Methylthiofentanyl, Thiofentanyl, Benzylfentanyl and Thenylfentanyl into schedule I of the CSA. This control action became effective on November 29, 1985.

These substances were emergency scheduled based on their appearance in the illicit market, their similarity in chemical structure to that of controlled substances, and the likelihood that they would produce pharmacological effects similar to those of prototypic schedule I or II substances. Often there is no biological data available prior to the emergency control of illicitly produced and abused substances. Therefore, information derived from structure-activity relationship considerations plays an important role in emergency scheduling. To keep an emergency scheduled substance in schedule I, DEA must initiate traditional scheduling procedures (21 U.S.C. 811) for that substance during the one year period in which it is emergency controlled and complete the action before the expiration of 18 months. The time limitations of emergency scheduling underscore the need for timely abuse liability data and the need to determine the most efficient tests to provide the data necessary to make permanent scheduling decisions. During the one-year temporary scheduling period, DEA must acquire sufficient data to make a determination as to whether the emergency scheduled substance should remain under the CSA. Often the substances have never been studied nor are they available for study. DEA, as soon as possible after identifying a newly abused substance, provides for the synthesis of this substance for analytical reference standards and biological testing. Only then can the appropriate pharmacological and abuse liability tests be conducted.

In an effort to assess the addiction liability of these compounds, DEA contracted studies of each of the temporarily scheduled fentanyl compounds at the University of Michigan Medical School in Ann Arbor and at the Medical College of Virginia in Richmond. The studies indicated that while most of the fentanyl compounds had abuse liability profiles that warranted control, two of these temporarily scheduled compounds (benzylfentanyl and thenylfentanyl) did not have an addiction-forming or addiction-sustaining liability similar to morphine.

Based on the results of these studies, on November 28, 1986, the DEA extended the temporary scheduling of six of these substances in schedule I. However, benzylfentanyl and thenylfentanyl were specifically omitted from this extension (and any future permanent control) because the pharmacological and biological testing of the substances, which included assessment of morphine-like activity, addiction liability, and analgesic effect, indicated that the compounds were both essentially inactive, with no evidence of abuse potential.

Both of these substances were temporarily controlled because they were initially found in street samples with other fentanyl analogues and were most likely unreacted intermediates in the synthesis of the target fentanyl analogues. The DEA, having concluded that these two drugs lacked morphine-like addictive properties, allowed the temporary regulation of benzylfentanyl and thenylfentanyl to expire on November 29, 1986. Therefore, these two substances were no longer regulated as controlled substances upon that date. In contrast, however, DEA chose to extend temporary control of the other four fentanyl compounds in a Final Rule published November 26, 1986 (51 FR 42834) and permanently controlled them in a Final Rule published May 29, 1987 (52 FR 20070).

Action of This Rulemaking

After the temporary listing of benzylfentanyl and thenylfentanyl expired in November of 1986, these compounds were no longer controlled under the CSA. However, DEA never deleted 21 CFR 1308.11(g)(1) and (g)(2) that reference the listing of these compounds temporarily in schedule I. This rulemaking hereby corrects the CFR to

delete 21 CFR 1308.11(g)(1) and (g)(2) which previously stated:

(1) N-[1-benzyl-4-piperidyl]-N-phenylpropanamide 9818 (benzylfentanyl), its optical isomers, salts and salts of isomers.

(2) N-[1-(2-thienyl)methyl-4-piperidyl]-N-phenylpropanamide 9834 (thenylfentanyl), its optical isomers, salts and salts of isomers.

This action therefore corrects part 1308 to remove any reference to control of benzylfentanyl and thenylfentanyl in schedule I.

Regulatory Certifications

[Editor's Note: See the Federal Register for all regulatory certifications.]

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is amended as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b) unless otherwise noted.

2. Section 1308.11 is amended by revising paragraph (g) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(g) Temporary listing of substances subject to emergency scheduling. Any material, compound, mixture or preparation which contains any quantity of the following substances:

(1) [Reserved.]

(2) [Reserved.]

Dated: June 19, 2010.

Michele M. Leonhart,
Deputy Administrator.

[FR Doc. 2010-15529 Filed 6-28-10; 8:45 am]

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- SCHEDULING UPDATE –

[Editor's Preface: The following notice has been edited for *Microgram Bulletin*. See the Federal Register: June 29, 2010 (Volume 75, Number 124) (Rules and Regulations) (Page 37301-37307) for the complete text of the ruling.]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1310

[Docket No. DEA-222F] RIN 1117-AA64

Exempt Chemical Mixtures Containing Gamma-Butyrolactone

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Final Rule.

SUMMARY: This rulemaking finalizes a November 12, 2008, Notice of Proposed Rulemaking in which DEA proposed that chemical mixtures that are 70 percent or less gamma-butyrolactone (GBL), by weight or volume, be automatically exempt from regulatory controls under the Controlled Substances Act (CSA). DEA is seeking through this rulemaking to exempt only those chemical mixtures that do not represent a significant risk of diversion. This regulation makes GBL chemical mixtures, in concentrations greater than 70 percent, subject to List I chemical regulatory requirements of the CSA, except if exempted through an existing categorical exemption. DEA is taking this action because there is a serious threat to the public safety associated with the ease by which GBL is chemically converted to the schedule I controlled substance gamma-hydroxybutyric acid (GHB).

DEA recognizes that concentration criteria alone cannot identify all mixtures that warrant exemption. As a result, DEA regulations provide for an application process by which manufacturers may obtain exemptions from CSA regulatory controls for those GBL chemical mixtures that are not automatically exempt under the concentration criteria.

DATES: This rulemaking becomes effective July 29, 2010. Persons seeking registration must apply on or before July 29, 2010 to continue their business pending final action by DEA on their application.

FOR FURTHER INFORMATION CONTACT: Christine A. Sannerud, PhD, Chief, Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, 8701 Morrissette Drive, Springfield, VA 22152; Telephone: (202) 307-7183.

SUPPLEMENTARY INFORMATION:

DEA's Legal Authority

DEA implements the Comprehensive Drug Abuse Prevention and Control Act of 1970, often referred to as the Controlled Substances Act (CSA) and Controlled Substances Import and Export Act (21 U.S.C. 801 et seq.), as amended. DEA publishes the implementing regulations for these statutes in Title 21 of the Code of Federal Regulations (CFR), parts 1300 to end. These regulations are designed to ensure that there is a sufficient supply of controlled substances for legitimate medical purposes and to deter the diversion of controlled substances to illegal purposes. The CSA mandates that DEA establish a closed system of control for manufacturing, distributing, and dispensing controlled substances. Any person who manufactures, distributes, dispenses, imports, exports, or conducts research or chemical analysis with controlled substances must register with DEA (unless exempt) and comply with the applicable requirements for the activity. The CSA as amended also requires DEA to regulate the

manufacture and distribution of chemicals that may be used to manufacture controlled substances. Listed chemicals that are classified as List I chemicals are important to the manufacture of controlled substances. Those classified as List II chemicals may be used to manufacture controlled substances.

Illicit Uses of Gamma-Butyrolactone

Gamma-Butyrolactone, or GBL, is a chemical that is used as a precursor in the illicit manufacture of the schedule I controlled substance gamma-hydroxybutyric acid, or GHB. GBL is a necessary and important chemical precursor in the clandestine synthesis of GHB because, to date, no other chemical has been identified as a substitute for GBL in the clandestine process. Congress recognized this and regulated GBL as a List I chemical upon enactment of Pub. L. 106-172, the Hillory J. Farias and Samantha Reid Date-Rape Drug Prohibition Act of 2000, on February 18, 2000.

GBL and GHB induce a sense of euphoria and intoxication and are abused for their central nervous system (CNS) depressant effect. An overdose from GBL or GHB may result in respiratory depression, coma, and even death. Both substances have been associated with drug- facilitated sexual assaults. The Drug Abuse Warning Network (DAWN) is a national surveillance system operated by the Substance Abuse and Mental Health Services Administration (SAMHSA) to monitor trends in drug emergency department visits. SAMHSA collects information on GHB and GBL separately but reports GHB and GBL together in its publications. This reflects the similar threat to public safety and abuse liability of GBL to GHB.

The conversion of GBL to GHB in a clandestine laboratory is a simple one-step process. Availability of GBL is the determining factor in producing GHB, not the execution of complicated chemical procedures or having sophisticated scientific equipment. GBL is a unique chemical precursor. It can be either converted into GHB by a simple chemical reaction or efficiently converted into GHB by the body upon ingestion, thus producing the same pharmacological effects as ingesting GHB. For this reason, abusers or predators seeking to use GBL on their victims routinely substitute GBL for GHB to obtain the same type of intoxication.

Other Laws That Apply to GBL: Controlled Substance Analogue Provisions

Section 802(32)(B) of Title 21 provides that the designation of GBL, or any other chemical, as a listed chemical does not preclude a finding that the chemical is a controlled substance analogue under subparagraph (A) of the definition 21 U.S.C. 802(32)(A).\1\ A controlled substance analogue is treated, for purposes of Federal law, as a schedule I controlled substance to the extent intended for human consumption (21 U.S.C. 813). The analogue provision of the CSA has been applied to prosecute individuals who have diverted GBL for human consumption. Although a chemical commodity when used by legitimate industry, diversion of GBL is tantamount to diversion of a schedule I controlled substance if intended for human consumption.

[\1\ 21 U.S.C. 802(32)(A) Except as provided in subparagraph (C), the term "controlled substance analogue" means a substance -- (i) The chemical structure of which is substantially similar to the chemical structure of a controlled substance in schedule I or II;
(ii) Which has a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II; or
(iii) With respect to a particular person, which such person represents or intends to have a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to or greater than the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance in schedule I or II.
(B) The designation of gamma butyrolactone or any other chemical as a Listed chemical pursuant to paragraph (34) or (35) does not preclude a finding pursuant to paragraph (A) of this paragraph that the chemical is a controlled substance analogue.]

Concern Over GBL-Containing Chemical Mixtures

Prior to control as a List I chemical, GBL had been sold under false pretenses to disguise its intended use. Suppliers pretended that GBL was being sold for use as ink jet printer cleaners, room deodorizers, and as educational kits (which purport to demonstrate the scientific principle of an exothermic chemical reaction).

Since the designation of GBL as a List I chemical in 2000, persons who manufacture, distribute, import, or export GBL must be registered with DEA and maintain records of transactions in GBL. These regulatory requirements prevent unscrupulous persons from freely distributing GBL. Persons without a legitimate business need to manufacture or distribute GBL do not receive the required registration from DEA. DEA believes that those wishing to traffic GBL are less willing to purchase GBL from DEA-approved registrants who are required to maintain records that are accessible to DEA.

DEA has observed the retail marketing and promotion of chemical mixtures containing GBL. Exempt chemical mixtures containing GBL were sold as cosmetic products and contained greater than 99 percent GBL (along with dye(s), fragrance(s), skin conditioners, and other ingredients). DEA became aware that persons were purchasing such products for conversion to GHB or directly ingesting these products for their GBL content. Retailers reported that they quickly sold out of these products. DEA notified retailers of the potential for abuse, which resulted in the voluntary withdrawal of these products from store shelves. Manufacturers of said products stated their intent to reformulate these products.

DEA is concerned that legitimate businesses may be unintentionally contributing to the diversion of GBL. Without regulatory controls, DEA is unable to monitor distributions of such chemical mixtures containing GBL, since registration and recordkeeping requirements do not apply. Regulation of GBL chemical mixtures pursuant to 21 U.S.C. 802(39)(A)(vi) is necessary to reduce the threat to the public health and safety.

Defining a Chemical Mixture

Title 21 U.S.C. 802(40) defines the term "chemical mixture" as "a combination of two or more chemical substances, at least one of which is not a List I chemical or a List II chemical, except that such term does not include any combination of a List I chemical or a List II chemical with another chemical that is present solely as an impurity." Therefore, a chemical mixture contains any number of listed chemicals in combination with any number of non-listed chemicals.

DEA does not consider a chemical mixture to mean the combination of a listed chemical and an inert carrier. An inert carrier is any chemical that does not modify the function of the listed chemical but is present to aid in the delivery of the listed chemical. Examples include, but are not limited to, dilutions in water and the presence of a carrier gas. For purposes of control under the CSA, these examples would be controlled as List I or List II chemicals, not as a chemical mixture containing a List I or List II chemical.

Past Regulations Regarding Chemical Mixtures

The Chemical Diversion and Trafficking Act of 1988 (Pub. L. 100- 690) (CDTA) created the legal definition of a "chemical mixture" (21 U.S.C. 802(40)), and exempted chemical mixtures from regulatory coverage. The CDTA established 21 U.S.C. 802(39)(A)(v) to exclude "any transaction in a chemical mixture" from the definition of a "regulated transaction." The result of such exemption was that it provided traffickers with an unregulated source for obtaining listed chemicals for use in the illicit manufacture of controlled substances.

The Domestic Chemical Diversion Control Act of 1993 (Pub. L. 103- 200) (DCDCA), enacted in April 1994, subjected all chemical mixtures containing List I and List II chemicals to CSA regulatory requirements, unless such chemical mixtures were specifically exempted by regulation. The regulatory requirements include recordkeeping, reporting, and security for all regulated chemical mixtures with the additional requirement of registration for handlers of List I chemical mixtures. The DCDCA also provided the Attorney General with the authority to establish regulations exempting chemical mixtures from the definition of a "regulated transaction," "based on a finding that the mixture is formulated in such a way that it cannot be easily used in the illicit production of a controlled substance and that the listed chemical or chemicals contained in the mixture cannot be readily recovered" (21 U.S.C. 802(39)(A)(vi)).

DEA treats all chemical mixtures containing List I and List II chemicals as non-regulated (upon the withdrawal of its proposed rule "Implementation of the Domestic Chemical Diversion Control Act of 1993 (DCDCA)" (59 FR 51887, October 13, 1994; withdrawn at 59 FR 63738, December 9, 1994)) until it promulgates a final rule that identifies chemical mixtures that are exempt for each List I and List II chemical. The withdrawal sought to prevent the immediate regulation of qualified chemical mixtures, which was not necessary and would impose an undue burden on industry. It also provided DEA the opportunity to gather information to implement regulations pursuant to 21 U.S.C. 802(39)(A)(vi).

In 2003, DEA published a Final Rule (68 FR 23195, May 1, 2003) that identified exempt mixtures containing the chemicals ephedrine, N- methylephedrine, N-methylpseudoephedrine, norpseudoephedrine, phenylpropanolamine, and pseudoephedrine, with an effective date of June 2, 2003. In a second Final Rule (69 FR 74957, December 15, 2004; corrected at 70 FR 294, January 4, 2005,) DEA promulgated regulations that

defined exempt chemical mixtures for 27 of the remaining 38 listed chemicals. The effective date was January 14, 2005. As gamma- butyrolactone (GBL) was not a listed chemical when DEA initiated this regulatory action in 1998, regulation of chemical mixtures containing gamma-butyrolactone was not addressed but was the subject of a separate regulatory action.

Regulations Regarding Chemical Mixtures Containing GBL

On July 19, 2002, DEA published in the Federal Register an Advance Notice of Proposed Rulemaking (ANPRM) (67 FR 47403; corrected at 67 FR 53842, August 19, 2002; corrected at 67 FR 56776, September 5, 2002) in anticipation of identifying GBL-containing chemical mixtures to exempt by regulation. The ANPRM invited interested persons to submit information related to legitimate formulations containing GBL, including the concentration of GBL in their mixtures. Comments received to that ANPRM provided information DEA used in its Notice of Proposed Rulemaking.

On November 12, 2008, DEA published a Notice of Proposed Rulemaking (73 FR 66815) which proposed the control of certain GBL chemical mixtures.

Defining Exempt Chemical Mixtures Containing GBL

In defining exempt chemical mixtures containing GBL for purposes of the proposed rule, the clandestine use of GBL and the requirements of 21 U.S.C. 802(39)(A)(vi) were heavily considered. The requirements described by statute do not allow for exemptions based on such factors as: (1) Manufacturers selling only to known customers, (2) the cost of the mixture, (3) the customer's knowledge of the product's chemical content, packaging, and/or such related topics. 21 U.S.C. 802(39)(A)(vi) requires DEA to establish an exemption based on the finding (1) that the mixture is formulated in such a way that it cannot be easily used in the illicit production of a controlled substance and (2) that the listed chemical or chemicals contained in the mixture cannot be readily recovered.

After examination of the comments on the ANPRM and after weighing the risk of diversion, on November 12, 2008 (73 FR 66815), DEA proposed a 70 percent concentration limit (by weight or volume) to identify GBL chemical mixtures that do not pose a significant risk of diversion. In that NPRM, DEA stated that it anticipated that chemical mixtures over 70 percent, as identified for use as protective coatings and films, will be automatically exempt pursuant to 21 CFR 1310.12(d)(2) ("Completely formulated paints and coatings"), which is being revised to clarify that film-forming agents are exempted. Additionally, the NPRM clarified that other chemical mixtures having concentrations of GBL over 70 percent may qualify for exemption via the application process (21 CFR 1310.13). DEA proposed a 70 percent concentration limit in an effort to prevent the automatic exemption of chemical mixtures with higher concentration limits such as solvent-based mixtures (e.g., cleaners or thinners) which DEA had concluded could be useful to traffickers.

Comments

[Editor's Note: See the Federal Register for comments received and DEA's response to said comments.]

Thresholds and Excluded Transactions for Regulated GBL Chemical Mixtures

The List I chemical GBL, as described in 21 CFR 1310.04(g)(1), does not have a threshold. Therefore, all transactions in regulated GBL chemical mixtures are regulated transactions. Certain transactions described in 21 CFR 1310.08 are excluded from the definition of a regulated transaction. These excluded transactions, as specified in 21 CFR 1310.08(d), are domestic, import, and export distributions of GBL weighing 4,000 kilograms (net weight) or more in a single container. This exclusion also applies to chemical mixtures.

Requirements That Apply to Regulated List I Chemical Mixtures

[Editor's Note: See the Federal Register for requirements that apply to regulated List I chemical mixtures.]

Regulatory Certifications

[Editor's Note: See the Federal Register for all regulatory certifications.]

List of Subjects in 21 CFR Part 1310

Drug traffic control, List I and List II chemicals, Reporting requirements.

For the reasons set out above, 21 CFR part 1310 is amended as follows:

PART 1310--RECORDS AND REPORTS OF LISTED CHEMICALS AND CERTAIN MACHINES

1. The authority citation for part 1310 continues to read as follows:

Authority: 21 U.S.C. 802, 827(h), 830, 871(b), 890.

2. Section 1310.09 is amended by adding new paragraph (k) to read as follows:

Sec. 1310.09 Temporary exemption from registration.

* * * * *

(k)(1) Each person required by sections 302 or 1007 of the Act (21 U.S.C. 822, 957) to obtain a registration to manufacture, distribute, import, or export regulated GBL-containing chemical mixtures, pursuant to sections 1310.12 and 1310.13, is temporarily exempted from the registration requirement, provided that DEA receives a properly completed application for registration or application for exemption on or before July 29, 2010. The exemption will remain in effect for each person who has made such application until the Administration has approved or denied that application. This exemption applies only to registration; all other chemical control requirements set forth in parts 1309, 1310, and 1313 of this chapter remain in full force and effect.

(2) Any person who manufactures, distributes, imports or exports a GBL-containing chemical mixture whose application for exemption is subsequently denied by DEA must obtain a registration with DEA. A temporary exemption from the registration requirement will also be provided for those persons whose applications for exemption are denied, provided that DEA receives a properly completed application for registration on or before 30 days following the date of official DEA notification that the application for exemption has been denied. The temporary exemption for such persons will remain in effect until DEA takes final action on their registration application.

3. Section 1310.12 is amended in the Table of Concentration Limits in paragraph (c) by adding gamma-butyrolactone in alphabetical order between "Ethylamine and its salts" and "Hydriodic acid" under List I chemicals and by revising paragraph (d)(2) to read as follows:

Sec. 1310.12 Exempt chemical mixtures.

(c) * * *

Table of Concentration Limits

	DEA chemical Code Number	Concentration	Special Conditions
List I Chemicals			
Gamma-Butyrolactone	2011	70% by weight or volume	

(d) * * *

(2) Completely formulated paints and coatings: Completely formulated paints and coatings are only those formulations that contain all of the components of the paint or coating for use in the final application without the

need to add any additional substances except a thinner if needed in certain cases. A completely formulated paint or coating is defined as any clear or pigmented liquid, liquefiable or mastic composition designed for application to a substrate in a thin layer that is converted to a clear or opaque solid protective, decorative, or functional adherent film after application. Included in this category are clear coats, top-coats, primers, varnishes, sealers, adhesives, lacquers, stains, shellacs, inks, temporary protective coatings and film-forming agents.

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Dated: June 18, 2010.

Michele M. Leonhart,
Deputy Administrator.

[FR Doc. 2010-15518 Filed 6-28-10; 8:45 am]

BILLING CODE 4410-09-P

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SELECTED REFERENCES

[The Selected References section is a compilation of recent publications of presumed interest to forensic chemists. Unless otherwise stated, all listed citations are published in English. Abbreviated mailing address information duplicates that which is provided by the abstracting service. Patents and Proceedings are reported only by their *Chemical Abstracts* citation number.]

1. Aturki Z, D'Orazio G, Rocco A, Bortolotti F, Gottardo R, Tagliaro F, Fanali S. **CEC-ESI ion trap MS of multiple drugs of abuse.** Electrophoresis 2010;31(7):1256-1263. [Editor's Notes: A method for the separation and determination of nine drugs of abuse, including amphetamines, cocaine, codeine, heroin, and morphine is presented. The CEC experiments were performed in fused silica capillaries (100 μm x 30 cm) packed with a 3 μm cyano derivatized silica stationary phase. Contact: Istituto di Metodologie Chimiche, Monterotondo Scalo, Consiglio Nazionale delle Ricerche, Rome, Italy.]

2. Maietti S, Castagna F, Molin L, Ferrara SD, Traldi P. **Cocaine adulterants used as marker compounds.** Journal of Mass Spectrometry 2009;44(7):1124-1126. [Editor's Notes: Cocaine samples have been analyzed in order to identify, on the basis of the adulterants contained therein, their possible production area and the mechanism by which they have been placed on the market. Contact: Forensic Toxicology and Antidoping Unit, University Hospital of Padova, 135121 Padua, Italy.]

3. Martino R, Malet-Martino M, Gilard V, Balayssac S. **Counterfeit drugs: Analytical techniques for their identification.** Analytical and Bioanalytical Chemistry 2010; No pp. yet given. [Editor's Notes: Presents title study. Contact: Universite de Toulouse, Toulouse Cedex 9 31062, France.]

Additional References of Possible Interest:

1. Collins M, Salouros H, Cawley AT, Robertson J, Heagney AC, Arenas-Queralt A. **$\delta^{13}C$ and $\delta^{2}H$ isotope ratios in amphetamine synthesized from benzaldehyde and nitroethane.** Rapid Communications in Mass Spectrometry 2010;24(11):1653-1658. [Editor's Notes: Presents title study. Contact: National Measurement Institute, Australian Forensic Drug Laboratory, Sydney, Australia.]

2. Green G, Thevis M, Trevorrow P. **Growth hormone: Barriers to the implementation of human growth hormone testing in sport.** Drug Testing and Analysis 2009;1(9-10):455-456. [Editor's Notes: Presents title study. Contact: Pacific Palisades Medical Group, USA.]

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THE JOURNAL/TEXTBOOK COLLECTION EXCHANGE

The Journal/Textbook Collection Exchange is a service intended to facilitate the transfer of unwanted journals and textbooks to forensic libraries or other *Microgram* subscribers. The current donations are listed below. The offers are First Come/First Serve (except **libraries have preference**). There are no charges to the requestor. Please provide a full mailing address in the request. **Important!:** Do not provide an address that irradiates mail!

CRC Handbook of Chemistry and Physics, 49th Edition (1968-1969)
Journal of Forensic Sciences:
- 1991: March (#2)
- 1992: January (#1), March (#2), July (#4), September (#5), November (#6)
- 1993: January (#1), March (#2), May (#3), July (#4), September (#5)
- 1998: September (#5)
- 2000: January (#1), March (#2), May (#3), July (#4), September (#5)
- 2001: Complete set
- 2002: Complete set
- 2003: Complete set
- 2004: Complete set
- 2005: Complete set
- 2006: Complete set
- 2007: January (#1), March (#2), November (#6)
- 2008: Complete set
- 2009: Complete set

Forensic Science Review:
- 1999: December (#2)
- 2000: January (#1-2)
- 2006: January (#1), July (#2)

Forensic Science International:
- 2004: July (#2-3), August (#1), October (#2-3), November (#1), December (#2-3), December (Supplemental)
- 2005: January (#1), January (#2-3), March (#2-3)

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THE DEA FY 2010 STATE AND LOCAL FORENSIC CHEMISTS SEMINAR SCHEDULE

The FY 2010 schedule for the State and Local Forensic Chemists Seminar is as follows:

September 13-17, 2010

The school is open only to forensic chemists working for law enforcement agencies. It is intended for chemists who have completed their agency's internal training program and have also been working on the bench for at least one year. There is no tuition charge. The course is held at the Hyatt Place Dulles North Hotel in Sterling, Virginia (near the Washington/Dulles International Airport). A copy of the application form is reproduced on the last page of this issue of *Microgram Bulletin*. Completed applications should be mailed to the Special Testing and Research Laboratory (Attention: J. Head) at 22624 Dulles Summit Court, Dulles, VA 20166. For additional information, call (703) 668-3349.

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SCIENTIFIC MEETINGS

Title: 2010 Southwestern Association of Forensic Scientists Annual Meeting
Sponsoring Organization: Southwestern Association of Forensic Scientists
Inclusive Dates: September 20 - 24, 2010
Location: Great Wolf Lodge (Grapevine, TX)
Contact Information: swafs2010@yahoo.com
Website: www.swafs.us

* * * * *

Title: Southern Association of Forensic Scientists Annual Fall Meeting
Sponsoring Organization: Southern Association of Forensic Scientists
Inclusive Dates: September 19 - 24, 2010
Location: Hollywood Casino Hotel (Tunica, MS)
Contact Information: See Website
Website: www.southernforensic.org

* * * * *

Title: 2010 Northwest Association of Forensic Scientists Meeting
Sponsoring Organization: Northwest Association of Forensic Scientists
Inclusive Dates: September 27 - October 1, 2010
Location: Crown Plaza Portland (Portland, OR)
Contact Information: See Website
Website: www.nwafs.org

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Title: 2010 Midwestern Association of Forensic Scientists 39th Annual Meeting
Sponsoring Organization: Midwestern Association of Forensic Scientists
Inclusive Dates: October 4 - 8, 2010
Location: Kansas City Marriott Downtown (Kansas City, MO)
Contact Information: See Website
Website: www.mafs.net

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Title: The 2010 NEAFS & NEDIAI Joint Meeting
Sponsoring Organization: North Eastern Association of Forensic Scientist and the New England Division IAI Program
Inclusive Dates: November 8 - 12, 2010
Location: Equinox Golf Resort and Spa (Manchester, VT)
Contact Information: NEAFS2010@gmail.com
Website: www.neafs.org

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DEA State and Local Forensic Chemist Seminar Application

Name: (PRINT NAME EXACTLY AS IT IS TO APPEAR ON CERTIFICATE)	Title:

Employer:

Your Office Mailing Address (include city, state, and zipcode):	Length of Service:

Business Telephone: ( ) -	Business Fax: ( ) -	Date of Application:

Email Address:

Education

College or University	Degree	Major

Please Check Which Techniques or Equipment Are Used in Your Laboratory

	Color Tests		UV
	Column Chromatography		IR
	Microcrystal Tests		CE
	Thin Layer Chromatography		GC/MS
	GC		IR
	HPLC		Other (please specify)

Indicate Analytical Problem(s) Nominee Would Like to Have Covered:

Choice of Seminar Dates:
1st Choice: 2nd Choice:

Laboratory Chief/Director:

Printed Name:_____ Signature: _____

Title: _____ Date: _____

Phone: _____